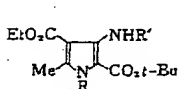
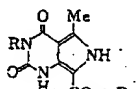


## Facile Synthesis of New Pyrrolo[3,4-d]pyrimidine-2,4-diones

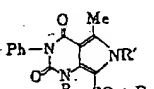
Recently we reported novel syntheses of certain new 3-aminoindoles, pyrrolo[3,2-b]indoles, pyrrolo[3,2-b]pyridines and pyrrolo[3,2-d]pyrimidines as well as of 3-aminopyrroles, e.g. 1.<sup>1)</sup> It is reasonable to predict that 1 can be converted to several pyrrolo[3,4-d]pyrimidine-2,4-diones containing a genuine pyrrole nucleus in the molecules via the corresponding ureas, such as 2 or 3, a conventional route, because 1 has a distinct structural feature suitable for the purpose. Since such pyrrolo[3,4-d]pyrimidinediones have never been prepared, they draw our attention by virtue of the structural relationship to 7- and 9-deazapurines. There has been no report of the use of 3-aminopyrroles for pyrrolo[3,4-d]pyrimidine synthesis;<sup>2)</sup> this is presumably due to the absence of good preparative method for 3-aminopyrroles. The ready availability of 1 facilitated us to fulfil the synthetic approach above suggested.<sup>3)</sup> We now wish to describe briefly the successful syntheses of new pyrrolo[3,4-d]pyrimidine-2,4-diones (4—10).



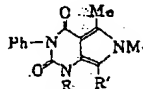
- 1: R=R'=H  
2: R=H, R'=CONHPh  
3: R=H, R'=CONHBz  
11: R=Me, R'=H



- 4: R=Ph  
5: R=Bz



- 6: R=H, R'=Me  
7: R=R'=Me



- 8: R=R'=H  
9: R=Me, R'=H  
10: R=Me, R'=CH2N(Me)2

Ph=phenyl

1 was heated in acetonitrile with phenyl or butyl isocyanate to obtain ureas 2, mp 232° and 3, mp 192—194°, respectively (each in 80% yield). When treated with NaOEt at room temperature, 2 and 3 underwent smooth cyclizations to give the expected products 4, mp 158—159°, ultraviolet (UV) spectrum  $\lambda_{\text{max}}$  nm (log  $\epsilon$ ): 240.5 (4.68) and 271.5 (4.28), infrared (IR) spectrum  $\nu_{\text{max}}$  cm<sup>-1</sup>: 1730, 1695 (shoulder) and 1675 (carbonyls), nuclear magnetic resonance (NMR) spectrum  $\delta$  (DMSO-*d*<sub>6</sub>): 12.20 (NH), 9.16 (NH), 7.1—7.4 (aromatic ring protons), 2.45 (CH<sub>3</sub>) and 1.57 (*tert*-C<sub>4</sub>H<sub>9</sub>), and 5, mp 194—196°, UV  $\lambda_{\text{max}}$  nm (log  $\epsilon$ ): 240 (4.51) and 271 (4.25), respectively each in 90% yield. Methylation of 4 with dimethyl sulfate-NaOH in aqueous methanol,<sup>4)</sup> or with dimethyl sulfate-K<sub>2</sub>CO<sub>3</sub> in dimethyl sulfoxide (DMSO) yielded 7, mp 230—231°, UV  $\lambda_{\text{max}}$  nm (log  $\epsilon$ ): 243 (4.52) and 280 (4.10), IR  $\nu_{\text{max}}$  cm<sup>-1</sup>: 1709, 1695 and

- 1) a) T. Murata, T. Segawara and K. Uekawa, *Chem. Pharm. Bull.* (Tokyo), 21, 2571 (1973); b) T. Murata and K. Uekawa, *ibid.*, 22, 240 (1974).  
2) For the known pyrrolo[3,4-d]pyrimidine syntheses, see F.L. Southwick, R. Madhav and J.A. Fitzgerald, *J. Heterocyclic Chem.*, 6, 507 (1969) and the literatures cited therein; B. Hansen and H. von Döbencz, *Ber.*, 105, 3630 (1972).  
3) In the preliminary report we stated that the yield of the 3-aminopyrrole derivative 1 was 70% based on the starting enaminonitrile<sup>1a)</sup>; however, scrutiny for the better reaction condition has raised the yield. Thus, methyl vinyl ketone (2 ml) was added at 15° to a mixture of the enaminonitrile (27 g) and NaOEt (prepared from 2.5 g of sodium) in ethanol (150 ml); the reaction mixture was stirred for 15 min, concentrated and diluted with water. The resulting crystals of 1 were collected, washed with water and dried. The product weighed 26.5 g (96%).  
4) G. Nübel and W. Pfeleiderer, *Ber.*, 98, 1060 (1965).